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## Mass production of systematic reviews and meta-analyses: an exercise in megasilliness?

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In 1978, the distinguished professor of psychology Hans Eysenck delivered a scathing critique of what was then a new method, that of meta-analysis, which he described as “an exercise in mega-silliness”. Based on a provocative essay by John Ioannidis in this issue of the journal<sup>1</sup>, “mega-silliness” may be an appropriate characterization of what the meta-analysis literature has become. According to surveys of the PubMed database and other empirical evaluations, Ioannidis paints a disturbing picture of the current state of affairs, where researchers are producing, in epidemic proportions, systematic reviews and meta-analyses that are redundant, misleading or serving vested interests.

Ioannidis presents an astounding case of 21 different meta-analyses of statins for atrial fibrillation in cardiac surgery published within a period of seven years, with some of these having practically identical results<sup>1</sup>. Moreover, his findings are in line with our recent cross-sectional study of systematic reviews of biomedical research<sup>2</sup>. We identified 682 systematic reviews indexed in MEDLINE® in a single month (February 2014), which is equivalent to 22 published per day. The majority of reviews did not consider study risk of biases or other reporting biases when drawing conclusions. Quality of reporting was highly variable: at least a third of reviews did not report use of a protocol, the search logic for at least one database, methods for data extraction and risk of bias assessment, or the funding source of the review. In addition, at least a third used statistical methods that are discouraged by leading systematic review organizations (e.g. the Cochrane Collaboration, The Agency for Healthcare Research and Quality’s (AHRQ) Evidence-based Practice Center program). Most concerning, there were generally only modest improvements in reporting over the last 10 years.

Why are so many systematic reviews and meta-analyses being produced? As Ioannidis demonstrates, a range of factors are at play here. Decision making bodies have a genuine

need to synthesize the ever expanding and conflicting biomedical literature on an ever increasing number of treatment options, in order to make evidence-based treatment recommendations. Researchers face pressures to publish (or perish) in order to advance their career. Journal editors recognize that publishing systematic reviews can help increase their impact factor, since they tend to be cited more than other types of studies. Industry employees can use the results of meta-analyses as a marketing device for their product. In addition, the plethora of biomedical journals provides researchers with many options to submit systematic reviews for publication, regardless of whether they are actually needed or performed rigorously and reported completely. This problem is likely to increase unless efforts are made to stop the growing number of “predatory journals”; businesses that pose as legitimate open-access publishers who charge publication fees to authors and in return publish anything quickly, with little or no peer review or quality control.

Why does the quality of systematic reviews and meta-analyses remain suboptimal? Despite best intentions, quality improvement initiatives have not had their desired impact. For example, in 2009, the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Statement was disseminated in leading medical journals to address the problem of poor reporting in reviews (<http://www.prisma-statement.org/>). However, endorsement of the guideline by journals is highly variable, with some editors only encouraging its use rather than implementing systems to monitor adherence, and many not referring to it at all. This may explain why we found only a third of systematic reviews explicitly referred to the use of PRISMA to guide reporting<sup>2</sup>. Further, some systematic reviews are conducted without any direct funding (13% in our sample). We do not know whether funded reviews are better conducted and reported than non-funded ones. Although it is possible that without specific

funding reviewers might be less inclined to adopt rigorous, time-consuming methods to focus their energies on funded projects.

Can anything be done to curb the mass production of redundant, misleading and conflicted systematic reviews and meta-analyses? We believe a number of strategies have potential. One is to make major changes to incentive structures in academia. Currently, academic promotion committees tend to weigh the number of publications an investigator has more heavily than features such as quality, impact and translational potential<sup>3</sup>. We suspect that research practices would change for the better if academics were rewarded for things like making their pre-specified analysis intentions publicly available, publishing articles that are more complete and transparent so that others are able to replicate the methods, and making the data and statistical analysis code available for reanalysis by independent investigators. This applies not just to systematic reviews and meta-analyses, but to all research studies. Policies to enhance transparency and reproducibility regarding the availability of data and methods for all research articles, which have been initiated by several journals, including *The Milbank Quarterly*, are also likely to improve the credibility of research articles in future.

One way to address the problem of misleading systematic reviews is to better educate biomedical researchers on research methodology and research waste<sup>4</sup>. Systematic reviews and meta-analyses are often conducted by authors with varied levels of formal training in clinical research methods. Education on these methodologies must become the norm, rather than the occasional venture, in all biomedical and public health curricula. Educational material should sensitize students to the myriad ways in which bias can be introduced into systematic review findings, and how to protect against these biases. Formal training in how to use reporting guidelines such as PRISMA should also be mandatory. This will, hopefully,

lead to a methodologically savvy scientific workforce, with strong concerns for the consequences that wasteful research can have on patient health and health care. Implementing these strategies will ultimately help reduce waste and increase the value of research<sup>4</sup>.

The redundancy of systematic reviews and meta-analyses highlighted by Ioannidis<sup>1</sup> could be addressed using the model of “living systematic reviews”. In this model, after completing an initial systematic review, a research community (comprising of collaborations between various players, such as scientists and citizen scientists) would regularly search for, screen, and select studies with new results, and if any exist, they would update the systematic review and meta-analysis with new data<sup>5</sup>. Rather than needlessly publishing multiple articles summarizing each update of the review, proponents of this model envisage a freely accessible website with live reporting of results to inform decision-making. We consider the recent extension of this concept to “living cumulative network meta-analyses”, which would allow for the simultaneous comparison of multiple interventions, and reduce the need for separate living meta-analyses addressing a single pairwise comparison<sup>5</sup>, an exciting development. By abolishing the need for systematic review publications, novel ways to acknowledge contributions (other than authorship) would need to be developed, and recognized in the academic incentive and reward structure. This approach might have a greater chance of gaining momentum if funding bodies supported this model of evidence gathering and academic institutions rewarded academics who participated in it.

No one group has prime responsibility for curbing the mass production of poor quality research, including systematic reviews and meta-analyses; to succeed, the strategies outlined above require enhanced collaboration between methodologists, clinical researchers, academic institutions, funding bodies, industry, journals and publishers. A scientific culture that values

methodological rigor, research transparency and data sharing over rampant productivity will hopefully produce systematic reviews that are necessary and non-duplicative, and that do not compromise on quality. As Ioannidis's essay clearly indicates, maintaining the status quo will not bring us closer to better value of research.

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